CHIRON

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Labor, Health and Human Services and Related Agencies
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Mr. Chairman, Members of the Committee: Thank you for the opportunity to provide a statement to the Appropriations Committee to address the critical importance of funding for pandemic preparedness. I am Dan Soland, President of Chiron Vaccines, one of the three divisions of Chiron Corporation, a U.S. biotechnology company headquartered in Emeryville, California. Chiron Corporations two other businesses are: BioPharmaceuticals and Blood Testing.

Chiron Overview

Chiron Vaccines is committed to the development and supply of vaccines to protect society against a range of important diseases, notably the possibility of a global influenza pandemic. We, and our predecessor companies, have a 100-year history in vaccine development and are the world's fifth-largest vaccines business with facilities located throughout Europe and Asia. Chiron Vaccines is the world's second-largest manufacturer of influenza vaccines and has important meningococcal, pediatric and travel vaccine franchises. We are the leading vaccine manufacturer in the United Kingdom, Germany and Italy. The company's portfolio of products includes vaccines for influenza, meningococcus C, rabies, tick-borne encephalitis, haemophilus influenzae B (Hib), polio, mumps, measles and rubella (MMR) and diphtheria, tetanus and pertussis (whooping cough).

Chiron and Pandemic Influenza

I welcome the opportunity to discuss with you the uncertain environment that the very real threat of a global influenza pandemic creates, and the importance of stabilizing our public health capacity and manufacturing infrastructure through public-private partnerships to save the lives of millions of Americans.

From Chiron's perspective as a manufacturer, we believe that there are three critical assets required for the U.S. to effectively prepare for pandemic influenza: technology and innovation; the development capability to turn technology into effective products; and the capital investment to deliver new technologies in the shortest time possible.

Technology and Innovation: Vaccine development against new and deadly viruses is a long and laborious process. The erosion of our domestic vaccine manufacturing capacity over the past decade has placed us in a precarious position relative to protecting public health. The most recent avian influenza concerns first arose NINE years ago, in 1997, when the H5N1 avian influenza virus moved from birds into humans. The evolution of this virus during the past nine years and its emergence outside of the Pacific Rim countries in the past several months has heightened concern about our preparedness to deal with a global influenza pandemic.

Chiron initiated innovative research on avian flu after the H5N1 outbreak in Hong Kong first affected humans. The high mortality of the H5N1 virus among birds, the quality that made it such a concern, also made it problematic to use in vaccine development—the virus tended to kill the chicken eggs that served as the first step of the vaccine production process. Chiron instead worked with a less pathogenic strain of H5 and consequently developed an H5N3 virus vaccine for testing against the H5N1 virus strain. Studies of this vaccine included Chiron's proprietary adjuvant,

MF59. An adjuvant is a substance that is added to a vaccine to enhance the body's immune response to the vaccine's active constituent, called the antigen. Our research found that, without the adjuvant, various tested doses of vaccine did not induce protective levels of antibodies. With the adjuvant, however, the vaccine induced protective antibody levels against the original H5N1 strain. Even at dose levels of 7.5 micrograms—half the dose of the seasonal influenza vaccine—protective levels were achieved. Importantly, people immunized with the adjuvanted vaccine in this trial showed protective antibody titers not just against the original H5N1 strain, but also against drifted strains of H5N1 that had changed over time.

These studies, reported in the peer-reviewed journals Lancet, Vaccine and the Journal of Infectious Diseases between 2001 and 2005, concluded that the use of Chiron's adjuvant MF59 in an avian flu vaccine may

- allow dose-sparing, in which using less vaccine per person would allow more people to be immunized, and
- offer cross-protection, in which the vaccine may offer protection against an avian flu virus even as it changed over time.

These findings must be validated by additional research. We were pleased with the validating research recently announced as a result of our collaboration with the National Institute of Allergy and Infectious Diseases (NIAID). In October 2005, Chiron reported promising data from an H9N2 study which found that all vaccine formulations containing MF59 were highly immunogenic, even at the lowest dose of 3.75 micrograms (a quarter of the dose used in seasonal flu vaccines). At the present time, we are collaborating with the NIAID to evaluate the use of this adjuvant in a trial of our H5N1 vaccine.

What is the lesson from Chiron's multi-year investment in pandemic vaccine research? Establishing the framework for the development of a pandemic vaccine is a long-term process that requires funding stability. Further, it is critically important the industry have the development capability to translate research into effective products.

Development Capability: Chiron has pushed the frontiers of science with the development of second-generation technologies for influenza vaccines. We believe we are on track to turn new technologies into innovative products with our adjuvanted vaccines and our second-generation influenza technology, Flu Cell Culture (FCC).

I have already addressed our track record in innovation for adjuvanted vaccines relative to pandemic influenza. Chiron has an adjuvanted vaccine, Fluad, which has been approved and on the market in several European countries for seasonal influenza for almost a decade. Experience with the use of this product in millions of Europeans positions us to apply our knowledge with adjuvanted vaccines to pandemic influenza development.

Additional technologies and innovation, such as FCC, are also critical to stabilize manufacturing capacity and rapidly respond to a global influenza pandemic. FCC vaccines represent the next generation of influenza vaccine production, both for annual vaccines and for long-term pandemic preparedness. FCC can provide significant advantages over traditional manufacturing methods by eliminating the dependence on chicken eggs for production. Removing egg supply lead times would

enable flexible and faster start-up of vaccine production in the event of an annual vaccine supply shortfall or an avian influenza pandemic.

Chiron has completed its second pivotal phase III enrollment in Europe for our FCC vaccine and plans to submit for E.U. regulatory approval in 2006. Chiron has a validated, full scale manufacturing facility for FCC in Marburg, Germany that is presently undergoing expansion in preparation for our launch in the EU. This fall we initiated our FCC development program in the U.S. with the launch of our Phase I/II research program. We are engaged with the U.S. regulatory authority, the Food and Drug Administration (FDA) and its advisory bodies, to structure the pathway for development and regulatory approval in the U.S.

Translating innovative technology into products on the market is not possible without a strong and well-resourced FDA. Over the past year, Chiron has had the opportunity to work closely with the men and women of the FDA as we proceeded through the remediation of our Liverpool facility. The FDA is to be commended for its professionalism, dedication and commitment to the vaccine industry. Having observed their dedication, it is regrettable that the funding for FDA under the recently enacted pandemic influenza supplemental appropriation is so limited. This agency will be pivotal in assuring that manufacturers can translate innovation into effective products and it is in the best interest of the U.S. that the FDA be appropriately funded to meet this important challenge. Mr. Chairman, Members of the Committee, this is one critical area where the government needs to provide additional resources to the FDA so they can carry out their mandate relative to pandemic preparedness.

The close collaboration of the FDA with European regulatory authorities enabled Chiron to supply influenza vaccine this season. In addition, HHS announced this past fall the award of a contract to Chiron for the production of pandemic influenza vaccine for the government's stockpile, which will be a critical source of vaccine supply in the early days of a pandemic. Production of the pandemic stockpile vaccine is underway now.

Capital Investment: The growing concern with regard to the inevitability of a global influenza pandemic, coupled with the erosion of our public health and manufacturing infrastructure in the U.S., creates a precarious situation as we develop the technologies, tools and policies to deal with pandemic influenza. We are engaged in a monumental undertaking that may save the lives of millions of Americans. It is critically important that the capital investment be available to deliver innovative technologies to the U.S. market in the shortest time possible. I should add that meeting the technical challenges required to prepare for a possible pandemic influenza outbreak entails significant business risks for manufacturers such as Chiron. Even with the support of the government, Chiron will be obliged to make a significant investment of time and money before it is able to realize any return on that investment. And there is no guarantee that Chiron will recover its costs or turn a profit on that investment.

The political resolve and will to create an environment of certainty for vaccine manufacturers is crucial to create U.S. vaccine manufacturing capacity and enable it to flourish. I appreciate the uncertainties that Congress faces associated with the "if" and "when" questions relative to a global pandemic juxtaposed against the need to be

fiscally responsible in tight economic times. However, we must have a sense of urgency—the U.S. vaccine capacity and our public health infrastructure has been eroded over several decades and they will not be restored in days, weeks or months. These assets will take years to rebuild.

Chiron Corporation strongly supported the Administration's funding request for pandemic influenza of $7.1 billion transmitted to Congress in November 2005. The Administration's request was structured to provide the Department of Health and Human Services (HHS) with the flexibility and resources to make the critical decisions about resource allocation to minimize the human and economic toll of pandemic influenza. Priorities that require full funding include:

- Improving our health care system capacity to identify and care for infected individuals;
- Global and national surveillance in order to allocate scare resources efficiently;
- International responsibilities to aid nations where H5N1 is endemic;
- Stockpiling to protect U.S. citizens; and
- The substantial challenge of restoring our vaccine industry in the U.S.

We appreciate that Congress provided a significant down payment on the Administration's request for HHS this past December as part of the Department of Defense Appropriations bill; however, the resources provided to HHS fell $3.4 billion short of the Administration's request. This shortfall did not send a positive message to manufacturers about the certainty and stability of the government efforts to fully address a public health threat of this magnitude. The message of certainty and stability for the U.S. vaccine manufacturing industry needs to be clear and unequivocal in light of its erosion in past years.

The Administration needs to include the remaining $3.4 B for HHS in their FY 07 funding proposal and Congress must find the resolve to fully resource this program. These funds are vitally important for competitive research programs; resources to fund the FDA and HHS's pivotal role in vaccine development and facility validation; and establishing and expanding domestic manufacturing capacity of second generation technologies, among other important priorities, so that pandemic preparations can be effectively resourced.

The government must engage in numerous public-private partnerships to maximize U.S. investment. Preparing for a global pandemic requires the consistent, committed and full collaboration of all vaccine manufacturers. A December 2005 report issued by the General Accounting Office (GAO) cites the potential for substantial economic impact as a result of a global pandemic. In its analysis, the GAO developed two models to estimate economic impact: severe and mild. The modeling for a severe pandemic indicates that the estimated decrease in "real GDP" of 4.7% exceeds the impact of every post WWII recession except the one following 1981. In the event of

a mild global pandemic, the impact on GDP will be significantly less; however, GAO has estimated that economic growth will slow.

We cannot afford to partially fund an effort of this magnitude—the human and economic consequences of inadequately preparing will be too grave. Of the three assets I described at the outset of my statement – technology and innovation; development capability; and capital investment – two are fully in place but the third, capital investment, is not fully present. Chiron stands ready to commit its scientific expertise, innovation and resources in collaboration with the government to engage in effective public-private partnership to ensure that the resources are available and the U.S. is positioned to meet this global challenge.

Conclusion

In closing, let me thank Congress for enacting legislation last year to address the critically important issue of pandemic influenza vaccine liability. We are grateful for the leadership of Congress and the Administration in addressing this issue. Pandemic vaccine products present unknown risks. Whatever regulatory approval mechanism might be adopted for pandemic vaccine in the event of an avian flu outbreak, it is likely that testing of the pandemic vaccine in humans will be less extensive than that for traditional flu vaccines. As a result, there may be limited data available on safety and adverse events before the vaccine is put into use. Additionally, it may be difficult to predict the numbers of people who would receive the pandemic vaccine -- in the event of a pandemic, the number could be far greater than the number currently vaccinated with the trivalent product, and could include subpopulations that would not normally be considered at high risk. For these reasons, any plan to prevent or treat pandemic influenza has the potential to present major liability risks to manufacturers and health care professionals. Products must be developed on an emergency basis and administered in a very short period of time to tens or hundreds of millions of people. The liability plan adopted by Congress was a critical first step in establishing a comprehensive liability program for pandemic influenza and Chiron looks forward to working with Congress to craft a compensation program to protect the interests of individuals who are immunized when a pandemic situation exists.

Mr. Chairman, this concludes my formal remarks and I will be happy to answer any questions you or the Committee might have for me. Thank you.